GEORGIA INSTITUTE OF TECHNOLOGY — OFFICE OF CONTRACT ADMINISTRATION

PROJECT ADMINISTRATION DATA SHEET

[x] ORIGINAL [ ] REVISION NO. ____

Project No. G-33-640 GTRI/GIT xxxx DATE 4/4/83

Project Director: Edward M. Burgess School/Lab xxxx Chem

Sponsor: DHHS/PHS/NIH/National Institute of General Medical Sciences

Type Agreement: Grant No. 1 R01 GM31930-01

Award Period. From 4/1/83 To 3/31/84 (Performance) 6/30/84 (Reports)

Sponsor Amount: Total Estimated: $ 94,239 Funded: $ 94,239

Cost Sharing Amount: $ 4,960 Cost Sharing No: G-33-343

Title: Acyclic Stereoselection

ADMINISTRATIVE DATA

OCA Contact Frank Huff

1) Sponsor Technical Contact:
Program Administrator
Dr. Carl A. Kuether
(301) 496-7181

2) Sponsor Admin/Contractual Matters:
Grants Management Specialists
Ms. Ann Calure/Mr. Jeff Carow
(301) 496-7166

Defense Priority Rating: NA

Military Security Classification: ____

(or) Company/Industrial Proprietary: ____

RESTRICTIONS

See Attached NIH Supplemental Information Sheet for Additional Requirements.

Travel: Foreign travel must have prior approval -- Contact OCA in each case. Domestic travel requires sponsor approval where total will exceed greater of $500 or 125% of approved proposal budget category.

Equipment: Title vests with Ga. Tech

COMMENTS:

COPIES TO:

Research Administrative Network
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~~Reports Coordinator (OCA)~~
GTRI
Library
Research Communications (2)
Project File
Other Burgess
Other ____

FORM OCA 4:781 (Rev 982)

GEORGIA INSTITUTE OF TECHNOLOGY OFFICE OF CONTRACT ADMINISTRATION

SPONSORED PROJECT TERMINATION/CLOSEOUT SHEET

Date 1/28/86

Project No. G-33-640 School/~~XXX~~ Chemistry

Includes Subproject No.(s) N/A

Project Director(s) Edward Burgess GTRC / ~~XXX~~

Sponsor

Title

Effective Completion Date: 3/31/84 (Performance) 6/30/84 (Reports)

Grant/Contract Closeout Actions Remaining:

- [ ] None
- [X] ~~XXXXXXXXXXXX~~ Final Fiscal Report
- [ ] Closing Documents
- [X] Final Report of Inventions 568 sent to Project Director.
- [ ] Govt. Property Inventory & Related Certificate
- [ ] Classified Material Certificate
- [ ] Other

Continues Project No. Continued by Project No. G-33-681

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FORM OCA 69.285

SECTION IV PROGRESS REPORT SUMMARY	GRANT NUMBER GM 31930-02	
PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR Burgess, Edward M.	PERIOD COVERED BY THIS REPORT FROM	THROUGH
NAME OF ORGANIZATION Georgia Institute of Technology	04/01/83	01/31/84

TITLE *(Repeat title shown in item 1 on first page)*

Acyclic Stereoselection

(SEE INSTRUCTIONS)

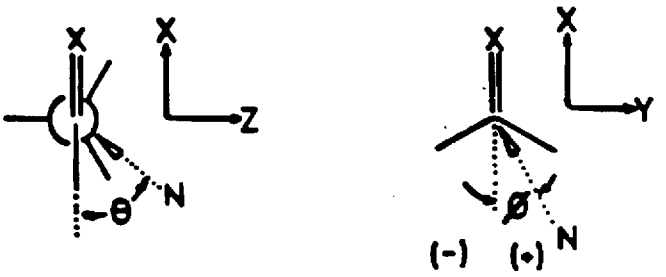
Publications:

C. L. Liotta, E. M. Burgess and W. H. Eberhardt, "Trajectory Analysis I. Theoretical Model for Nucleophilic Attack at Pi-Systems. The Stabilizing and Destabilizing Orbital Terms.", J. Am. Chem. Soc., in press (1984).

Report:

Theoretical Model.

A simple model has been been developed for qualitatively describing the trajectory along the reaction coordinate of an attacking nucleophile at a pi-electrophilic center in terms of the minimum energy trajectory angles θ and ϕ and the reaction windows W_θ and W_ϕ associated with each of these (Figure).

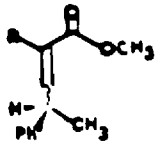
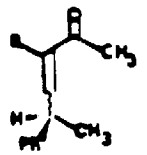
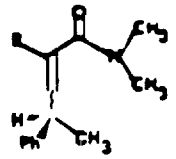


The above parameters provide information pertaining to certain stereochemical properties, such as asymmetric induction, to be expected from a reacting system. The model is presently being expanded to include the effects of nucleophile charge on the polarization of the pi-electrophile and the relationship of this polarization to the minimum energy trajectory angles (θ, ϕ) and windows (W_θ, W_ϕ).

Asymmetric Induction in Michael Addition Reactions Using Organocuprate Reagents.

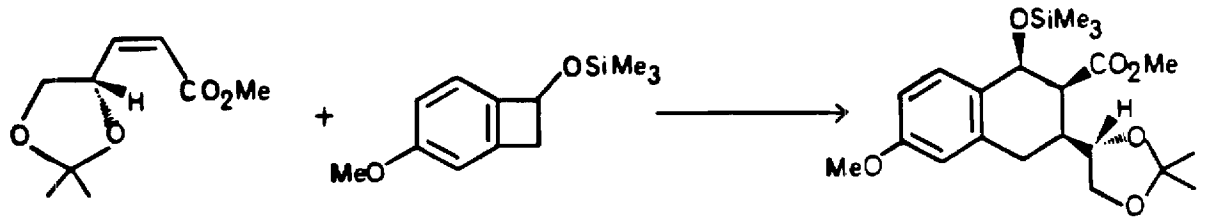
Twelve α,β-unsaturated carbonyl substrates were prepared with chiral centers located at the β-position. These included cis and trans enoates, enones and enamides. Each of the substrates was allowed to react with lithium dimethylcuprate to form a pair of diastereomeric products. The trajectory model predicted that nucleophilic attack at the β-position would show greater diasteriomeric selectivity for the cis isomer as compared to the trans counterpart. The results are summarized in the Table. In all cases, the cis isomer did give greater diasterioselectivity than the corresponding trans isomer in agreement with the theoretical predictions.

Table. Ratio of Major Pair to Minor Pair for Cuprate Additions

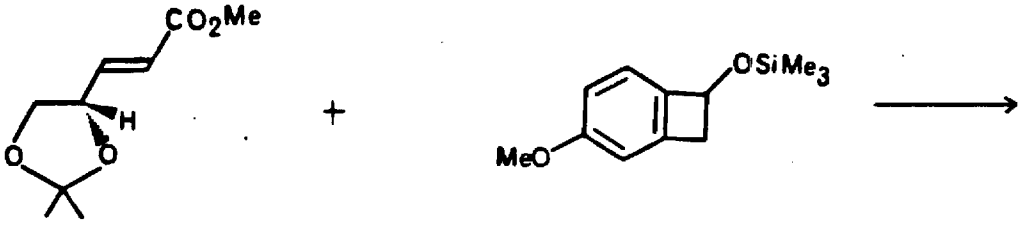
	R = H		R = CH_3	
	cis	trans	cis	trans
	6.18:1.00	3.21:1.00	5.74:1.00	3.45:1.00
	3.25:1.00	2.91:1.00	3.01:1.00	3.11:1.00
	2.39:1.00	2.00:1.00	2.14:1.00	2.08:1.00

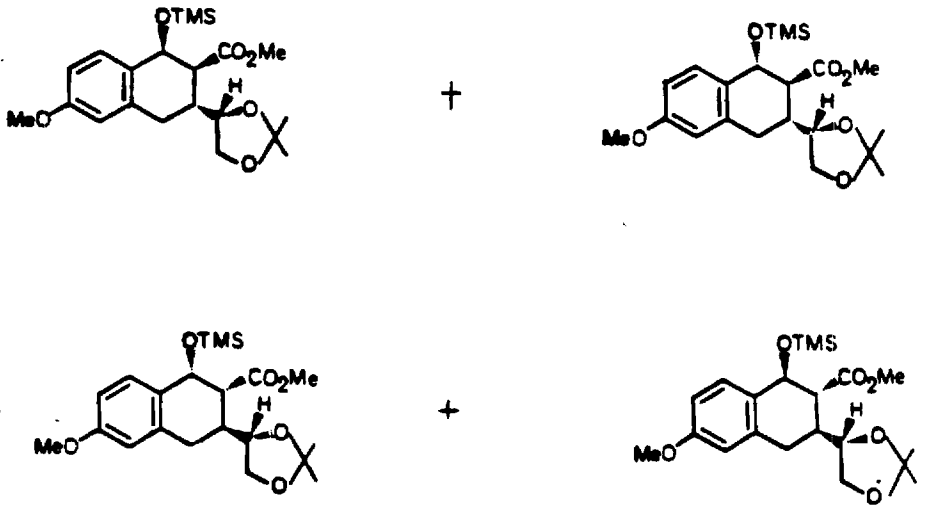
Asymmetric Induction in Intermolecular Diels-Alder Reactions.

The asymmetric induction accompanying reaction at the β-position of an α,β-unsaturated carbonyl system has been extended to the Diels-Alder reaction. The E and Z isomers of R-methyl-4-(2,2-dimethyl-1,3-dioxolanyl)-2-propenoate have been synthesized and reacted with 1-trimethylsiloxy-5-methoxybenzocyclobutane accompanying thermal ring openning. Reaction of the Z isomer resulted in formation of one adduct as 95% of the reaction products. A single crystal X-ray analysis was conducted on this product.



The E isomer, on the other hand, gave four major products: the two endo adducts and the two exo adducts each in a 2.2:1 ratio.

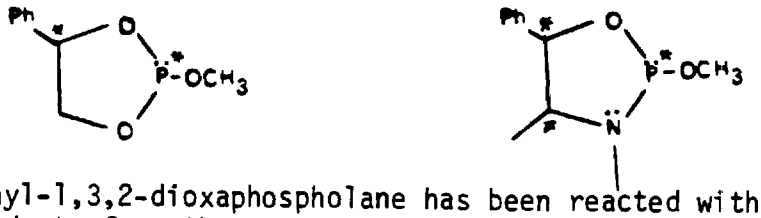




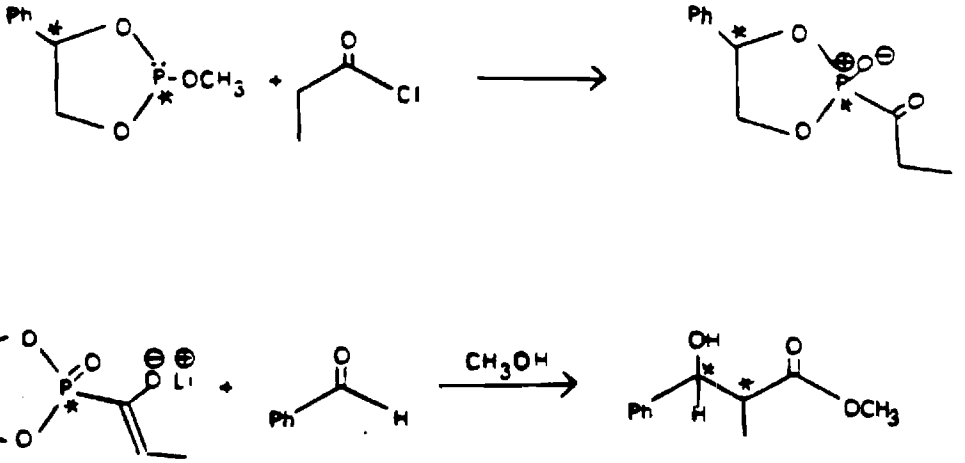
The above results are again in agreement with the prediction of the trajectory model discussed earlier.

Synthesis of Chiral Auxilliary Substituents.

The following chiral phosphorus(III) species have been synthesized in order to ascertain their effectiveness as chiral auxilliary substituents when transformed into enolizable acylphosphine oxides by means of reaction with acid chlorides (Arbusov Reaction).



2-Methoxy-4-phenyl-1,3,2-dioxaphospholane has been reacted with acetyl chloride and propionyl chloride to form the corresponding acylphosphine oxide from which the "rigid" lithium enolate is formed. The asymmetric induction accompanying the reaction of this chiral enolate with a variety of aldehyde substrates is presently under investigation.



The reaction of 3,4-dimethyl-2-acetyl-5-phenyl-],3,2-oxazophospholidine with acid chlorides produced a complex mixture of products. The cyclohexyl counterpart of 2-methoxy-4-phenyl-],3,2-dioxaphospholane is presently being prepared. It is believed that the cyclohexyl substituent will provide greater asymmetric induction than the corresponding phenyl substituent.